IN THE SPECIFICATION

Please **amend** paragraph [0003] on pages 3-4 as follows:

Pre-mRNA splicing proceeds by a two-step mechanism. In the first step, the 5' splice site is cleaved, resulting in a "free" 5' exon and a lariat intermediate (Moore, M.J. and P.A. Sharp, 1993, *Nature* 365:364-368). In the second step, the 5' exon is ligated to the 3' exon with release of the intron as the lariat product. These steps are catalyzed in a complex of small nuclear ribonucleoproteins and proteins called the spliceosome. The splicing reaction sites are defined by consensus sequences around the 5' and 3' splice sites. The 5' splice site consensus sequence is AG/GURAGU (SEQ ID NO:1) (where A=adenosine, U = uracil, G = guanine, C = cytosine, R = purine and / = the splice site). The 3' splice region consists of three separate sequence elements: the branch point or branch site, a polypyrimidine tract and the 3' splice consensus sequence (YAG). These elements loosely define a 3' splice region, which may encompass 100 nucleotides of the intron upstream of the 3' splice site. The branch point consensus sequence in mammals is YNYURAC (SEQ ID NO:2) (where N = any nucleotide, Y= pyrimidine) . The underlined A is the site of branch formation (the BPA = branch point adenosine). The 3' splice consensus sequence is YAG/G. Between the branch point and the splice site there is usually found a polypyrimidine tract, which is important in mammalian systems for efficient branch point utilization and 3' splice site recognition (Roscigno, R., F. *et al.*, 1993, *J. Biol. Chem.* 268:11222-11229). The first YAG trinucleotide downstream from the branch point and polypyrimidine tract is the most commonly used 3' splice site (Smith, C.W. *et al.*, 1989, *Nature* 342:243-247).

Please **amend** paragraph [0022] on page 10 as follows:

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Figure 4. Diagram and important structural elements of double *trans*-splicing PTM7. The double splicing PTM7 has both 3' and 5' functional splice sites as well as binding domains (SEQ ID NOS:11-17).

Please **amend** paragraph [0025] on page 11 as follows:

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Fig. 6C. The accuracy of double *trans*-splicing of synthetic PTM RNA in 293T cells was verified by sequencing the spliced RNA produced by RT-PCR (SEQ ID NOS:18 and 19).

Please **amend** paragraph [0035] on pages 15-16 as follows:

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The PTM molecule also contains a 3' splice region that includes a branch point, pyrimidine tract and a 3' splice acceptor AG site and/or a 5' splice donor site. Consensus sequences for the 5' splice donor site and the 3' splice region used in RNA splicing are well known in the art (See, Moore, *et al.*, 1993, The RNA World, Cold Spring Harbor Laboratory Press, p. 303-358). In addition, modified consensus sequences that maintain the ability to function as 5' donor splice sites and 3' splice regions may be used in the practice of the invention. Briefly, the 5' splice site consensus sequence is AG/GURAGU (SEQ ID NO:1) (where A=adenosine, U=uracil, G=guanine, C=cytosine, R=purine and /=the splice site). The 3' splice site consists of three separate sequence elements: the branch point or branch site, a polypyrimidine tract and the 3' consensus sequence (YAG). The branch point consensus sequence in mammals is YNYURAC (SEQ ID NO:2) (Y=pyrimidine). The underlined A is the site of branch formation. A polypyrimidine tract is located between the branch point and the splice site acceptor and is important for different branch point utilization and 3' splice site recognition.

Please **amend** paragraph [0041] on pages 17-18 as follows:

A nucleotide sequence encoding a translatable protein capable of producing an effect, such as cell death, or alternatively, one that restores a missing function or acts as a marker, is included in the PTM of the invention. For example, the nucleotide sequence can include those sequences encoding gene products missing or altered in known genetic diseases. Alternatively, the nucleotide sequences can encode marker proteins or peptides which may be used to identify or image cells. In yet another embodiment of the invention nucleotide sequences encoding affinity tags such as, HIS tags (6 consecutive histidine residues) (Janknecht, et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972-8976), the C-terminus of glutathione-S-transferase (GST) (Smith and Johnson, 1986, Proc. Natl. Acad. Sci. USA 83:8703--8707) (Pharmacia) or FLAG (Asp-Tyr-Lys-Asp-Asp-Asp-Lys) (SEQ ID NO:3) (Eastman Kodak/IBI, Rochester, NY) can be included in PTM molecules for use in affinity purification. The use of PTMs containing such nucleotide sequences results in the production of a chimeric RNA encoding a fusion protein containing peptide sequences normally expressed in a cell linked to the peptide affinity tag. The affinity tag provides a method for the rapid purification and identification of peptide sequences expressed in the cell. In a preferred embodiment the nucleotide sequences may encode toxins or other proteins which provide some function which enhances the susceptibility of the cells to subsequent treatments, such as radiation or chemotherapy.

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Please **amend** paragraph [0060] on page 25 as follows:

Alternatively, synthetic PTMs can be generated by *in vitro* transcription of DNA sequences encoding the PTM of interest. Such DNA sequences can be incorporated into a wide variety of vectors downstream from suitable RNA polymerase promoters such as the T7, SP6, or

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T3 polymerase promoters. Consensus RNA polymerase promoter sequences include the following:

T7: TAATACGACTCACTATAGGGAGA (SEQ ID NO:4)

SP6: ATTTAGGTGACACTATAGAAGNG (SEQ ID NO:5)

T3: AATTAACCCTCACTAAAGGGAGA. (SEQ ID NO:6)

The base in bold is the first base incorporated into RNA during transcription. The underline indicates the minimum sequence required for efficient transcription.

Please **amend** paragraph [0092] on pages 37-38 as follows:

Total cell RNA (2.5 μg) from the transfections was converted to cDNA using the MMLV reverse transcriptase enzyme (Promega) in a 25 μl reaction following the manufacturers protocol with the addition of 50 units RNase Inhibitor (Life Technologies) and 200 ng Lac-6R gene specific primer:

(5'-CTAGGCGGCCGCCTGCTGGTGTTTTGCTTCC) (SEQ ID NO:7).

cDNA synthesis reactions were incubated at 42°C for 60 min followed by incubation at 95°C for 5 min. This cDNA template was used for PCR reactions. PCR amplifications were performed using 100 ng primers and 1 μl template (RT reaction) per 50 μl PCR reaction. A typical reaction contained ~25 ng of cDNA template, 100 ng of primers (common to cis- and trans-spliced products) (KI-1F, 5'-GTTTCGCTAAATACTGGCAGG and, Lac-6R, 5'-CTAGGCGGCCGCCTGCTGGTGTTTTGCTTCC) (SEQ ID NOS: 8 and 9) 1X REDTaq PCR buffer (10 mM Tris-HCl, pH 8.3, 50 mM KCl, 1.1 mM $MgCl_2$ and 0.1% gelatin), 200 μM dNTPs and 1.5 units of REDTaq DNA polymerase (Sigma, Saint Louis, Missouri). PCR reactions were performed with an initial pre-heating at 94°C for 2 min 30 sec followed by 20 cycles of 94°C for 30 sec (denaturation), 60°C for 36 sec (annealing) and 72°C for 1 min

(extension) followed by a final extension at 72°C for 7 min. The PCR products were then digested with Sph I and Dde I restriction endonucleases, which specifically cleaves cis-spliced product. Trans-spliced product was isolated using Lac-21 (has biotin at the 5' end) as a hybridization probe. The purified trans-spliced product was subjected to a 2nd round of nested PCR using primers KI-2F (5'-CTGGCAGGCGTTTCGTCAG) (SEQ ID NO:10) and Lac-6R. Authenticity of the trans-spliced product was further confirmed by diagnostic digestion with Pvu I restriction enzyme which specifically cleaves the trans-spliced product.